REMARKS

Reconsideration is respectfully requested in view of Applicant's amendments and remarks herein.

Applicants affirm their election of Group II, claims 18-24 for prosecution at this time. With respect to the traversal, Applicants submit that for an examination of the Group II composition claims which are directed to the use of a D-serine transport inhibitor for treating schizophrenia, that the method claims which are corresponding claims 1-17 would also need to be examined.

At the middle of page 3 of the Office Action, claims 18-24 are rejected under the judicially created doctrine of double patenting over claims 1-20 of U.S. Patent 6,361,957. Applicants respectfully request reconsideration.

The relevant claims of the '957 patent are directed to an assay method, while the claims under consideration of the present invention are directed to a composition for treating schizophrenia. There is no relationship whatsoever between these two sets of claims. Without question, claims 18-24 of the present application cannot be considered to be obvious over claims 1-20 of the '957 patent. Accordingly, reconsideration of the double patenting rejection is requested. Even so, Applicants submit herewith a Terminal Disclaimer to advance prosecution.

At the middle of page 4 of the Office Action, claims 20-24 are rejected under the first paragraph of 35 U.S.C. § 112, as being non-enabling.

Applicants disagree that the specification is not enabling for one with ordinary skill in the art. Construction of compound libraries based upon functional assays is a standard chemical

approach. Since submission of the original application, using the concept of claims 22 and 23, Applicant has obtained a library consisting of over 200 compounds meeting the specification (hydrophobic group attached to either the C or N of D-serine), as illustrated in the appendix. Several of these compounds have shown ability to inhibit D-serine transport using the assay system described herein. Generation of these compounds was performed by one of ordinary skill in the art, and testing was performed according to specifications provided. Thus, the specification has proven enabling to individuals skilled in the art, contrary to assertions of the Examiner.

In summary, since the skilled artisan can readily determine derivatives of serine or alanine usable in the present invention, Applicant's claims 20-24 are clearly enabled by the application as filed.

At the top of page 5 of the Office Action, claims 18-23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Applicant's admissions. As best as understood, it is believed that the Examiner's position is that D-serine, known in the art, acts as a D-serine transport inhibitor.

Applicant respectfully submits the Examiner's assertion that D-serine and D-serine transport inhibitors speak to the same effect is incorrect. D-serine binds directly to the glycine/D-serine binding site of the NMDA receptor complex to activate NMDA receptors. D-serine transport inhibitors, as described, do not bind to the glycine/D-serine binding site and thus do not substitute directly for D-serine. Instead, they inhibit reuptake of D-serine by D-serine transporters in brain. A novel inventive step of this application was the first

demonstration by the inventor of transporters capable of regulating D-serine concentrations in vivo.

On page 2, line 12 to page 3, lines 1-2, a clear distinctions is set forth between the concept of "agents that activate the glycine site directly (e.g., glycine, D-serine)" and agents that function "by inhibition of glycine or D-serine transport (e.g., D-ala dodecylamide)." An inventive concept underlying both this and prior applications is that the brain must contain transporters that regulate endogenous levels of glycine and D-serine even though these had not been described prior to Applicant's researches. Applicant's discovery in 1995 of a novel glycine transporter led to invention of the use of glycine transport inhibitors in treatment of schizophrenia (US patent 5,837,730 - Treatment of negative and cognitive symptoms of schizophrenia with glycine uptake antagonist). At the time those studies were conducted, no D-serine transporters had yet been described. The present application is the first to describe a novel D-serine transport process in the brain. Prior to demonstration of this transporter, development of D-serine transport inhibitors would have been impossible. This invention enables development of D-serine transport inhibitors and their use in schizophrenia.

Applicant disagrees with the Examiner on two accounts. First, the statement that Applicant has merely "discovered" the mechanism of therapeutic effect of D-serine is incorrect. D-serine does not function as a D-serine transport inhibitor since by definition it is transported by the D-serine transporter. This is obvious based upon Example 1, Figs. 1-3, of the application as filed in which uptake of D-[3H] serine is the primary variable being studied. If D-serine were a D-serine transport inhibitor it would not, by definition, be transported by the D-serine

transporter. Further, as demonstrated in these figures, uptake of unlabeled D-serine is able to compete with uptake of D-[3H]serine to reduce total tritium uptake to non-specific levels. The competitive nature of the interaction between tritiated [3H] and non-tritiated forms of D-serine is the hallmark of a competitive transport process. Such transport is not demonstrable for D-serine derivatives that function as D-serine transport inhibitors.

Because use of D-serine transport inhibitors is not taught by the prior art, use of D-serine transport inhibitors in combination with antipsychotics (claim 21) is also not taught by the prior art and is novel.

Applicants respectfully submit that the present application is in condition for allowance. If any minor points remain, the Examiner is respectfully requested to contact the undersigned at the below listed phone number.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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